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The Effect of Hochu-ekki-to on Aqueous Flare Elevation after Small-Incision Cataract Surgery

Shoichi Mizoguchi* **and Noriaki Chinen**

Konosu Station Mizoguchi Eye Clinic, Japan

***Corresponding author:** Shoichi Mizoguchi, Konosu Station Mizoguchi Eye Clinic, 1-1-3, Honcho, Konosu-shi, Saitama 365-0038, Japan, Tel: (+81) 48-540-2200; E-mail: shoenjoy@aol.com

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Abstract

Background: In Japan, Kampo medicines (Japanese herbal medicines) are often used as adjuvant therapy to Western medicines. In the present study, the effect of Kampo medicine Hochu-ekki-to (HOT) on aqueous flare elevation (AFE) after small-incision cataract surgery (SICS) was investigated.

Materials and methods: Fifteen patients (24 eyes) with age-related cataracts that underwent SICS were prospectively studied. Patients with glaucoma, diabetes, or uveitis were excluded from the study. HOT was orally administered to seven subjects (12 eyes) from the day of surgery through postoperative week 4. Control group subjects (eight subjects; 12 eyes) did not receive HOT. Both groups received the same nonsteroidal, steroidal, and antibacterial eye drops before and after surgery. AFE was measured preoperatively and postoperatively.

Results: AFE at postoperative weeks 2 and 4 was significantly lower in the HOT group than in the control group.

Conclusion: These results suggest that HOT is effective in suppressing AFE.

Keywords: Hochu-ekki-to; Kampo; Aqueous flare; Small incision; Age-related cataract

Introduction

Cataract is a condition in which the crystalline lens of the eye becomes cloudy due to age, congenital causes, injury, or diabetes. Cataract symptoms include blurred or double vision and decreased visual acuity. The frequency of cataract increases with age [1]. Medication can only delay cataract progression, whereas surgery is required to improve cataract symptoms. Marked advances in cataract surgery in recent years, such as phacoemulsification aspiration (PEA) and foldable intraocular lens implantation with small incision, have reduced patient burden and made comfortable postoperative visual function recovery possible. However, excessive postoperative inflammation can cause cystoid macular edema (CME) or secondary cataract [2,3]. Nonsteroidal anti-inflammatory eye drops that reduce postoperative inflammation can help prevent CME to some extent [4], however, a greater reduction in postoperative inflammation could help prevent both CME and secondary cataracts.

In Japan, Kampo medicines (Japanese herbal medicines) are approved for medical use and often used as adjuvant therapy to Western medicines. Hochu-ekki-to (HOT), which is effective against a weak constitution, fatigue, weakness after illness, poor appetite, and night sweats, is a Kampo medicine used clinically for physical recovery in postoperative and elderly patients. One of the basic pharmacological properties of HOT is cytokine regulation [5]. Because cytokines contribute to inflammation after cataract surgery [6], it was anticipated that HOT would help reduce inflammation after cataract surgery. In general, eye drops are used for post-cataract surgery management. HOT is administered orally and is therefore less of a burden on patients. Aqueous flare is often measured as follow-up for inflammation after cataract surgery [7,8]. In the present study, it was investigated whether HOT had effects on aqueous flare after cataract surgery by comparing it with a non-administration control group.

Material and Methods

Patients and Hochu-ekki-to administration

Fifteen patients (24 eyes; aged 70.3 ± 10.3 years) with age-related cataracts who underwent PEA and intraocular lens implantation were prospectively studied at the study hospital between July and December 2012. Patients with glaucoma, diabetes mellitus, or uveitis were excluded from the study. After receiving written consent, subjects were assigned to a group that received HOT (7 subjects, 12 eyes; HOT group) or a group that did not receive HOT (8 subjects, 12 eyes; control group). HOT was administered orally at 7.5 g/day with a half-dose taken twice daily from the day of surgery through postoperative week 4.

Hochu-ekki-to

HOT was purchased from Kracie Pharma, Ltd., Tokyo. HOT in 7.5 g contained hot water extract (6.4 g) from 10 species of medicinal plants including Ginseng radix (4.0 g), Atractylodis rhizome (4.0 g), Astragali radix (4.0 g), Angelicae radix (3.0 g), Zizyphi fructus (2.0 g), Bupleuri radix (2.0 g), Glycyrrhizae radix (1.5 g), Zingiberis rhizoma (0.5 g), Cimicifugae rhizoma (1.0 g), and Aurantii nobilis Pericarpium (2.0 g).

Cataract surgery

The same surgeon performed a standardized cataract surgery on all subjects. After performing a 2.8 mm upward incision into the cornea, PEA was performed and acrylic intraocular lenses (YA60BBR, Hoya Corporation, Tokyo, Japan) were implanted. The following eye drops were administered to all subjects: 0.5% levofloxacin hydrate (Santen Pharmaceutical Co., Ltd, Osaka, Japan) from 4 days before surgery to the day of surgery, 0.3% ofloxacin (WAKAMOTO Pharmaceutical Co., Ltd, Tokyo, Japan), 0.1% diclofenac sodium (WAKAMOTO), 0.1% dexamethasone metasulfobenzoate sodium (Nitto medic Co. Ltd, Toyama, Japan) from postoperative day 1 to week 3, 0.1% diclofenac sodium (WAKAMOTO), and 0.1% fluorometholone (Santen) from postoperative weeks 3 to 4.

Aqueous flare measurement

Aqueous flare was measured using a laser flare meter (Laser Flare Meter FM-600, Kowa Co., Ltd., Aichi, Japan) and was performed preoperatively and postoperatively on days 1 and 3 and weeks 1, 2, and 4. Five measurements were performed at each time point, and the mean value was calculated.

Statistical analysis

Results are presented as the mean ± standard deviation. A student's t test was used to statistically compare age, surgery time, crystalline lens hardness, ultrasound (U/S) time, and irrigation amount between groups. Gender-related differences were analyzed using the chi-square test. Aqueous flare results were analyzed using the Welch's t-test. The significance level was set at $p<0.05$.

Results and Discussion

No statistically significant difference was observed in age (75.6 ± 6.9 in the HOT, 65.8 ± 10.9 in the control) and sex (4 eyes of males and 8 eyes of females in HOT, 2 eyes of males and 10 eyes of females in control) between study groups. Table 1 shows the surgical parameters. No significant differences were noted between the HOT and control groups for surgery time, crystalline lens hardness, U/S time, or irrigation amount (Table 1).

	Control(n=12)	Hochu-ekki-to(n=12)	Statistical analysis
Surgery time(minutes)	16.1 ± 4.4	15.1 ± 3.5	p>0.05
Crystalline lens hardness(grade)	2.7 ± 0.7	3.0 ± 0.7	p>0.05
Ultrasound time(sec)	81.7 ± 19.1	96.9 ± 22.7	p>0.05
Irrigation amount(ml)	105.0 ± 39.0	117.5 ± 47.5	p>0.05
Results are presented as the mean ± standard deviation. Statistical analysis was performed using Student's t-test			

Table 1: Surgical conditions.

Figure 1 presents the pre- and post-operative aqueous flare levels for both groups. No significant differences were observed in the aqueous flare levels between the control and HOT groups on preoperative and postoperative days 1 and 3 and week 1. However, aqueous flare elevation was significantly lower in the HOT group than in the control group at postoperative weeks 2 and 4.

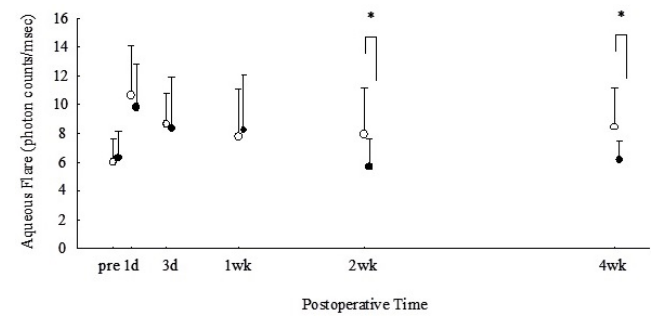

Figure 1: Effect of Hochu-ekki-to on aqueous flare elevation after small incision cataract surgery. ○, Control group (n=12); •, Hochu-ekki-to group (n=12). Results are presented as the mean ± standard deviation. Statistical analysis was performed using Welch's t-test (*$p<0.05$).

In recent years, advances in cataract surgery have made same-day surgery mainstream. These advances have reduced patient burden, but they have made management of postoperative complications, such as postoperative inflammation, even more important. In the present study, aqueous flare elevation after cataract surgery was compared between the HOT and control groups. The results indicated that aqueous flare elevation was significantly lower in the HOT group than in the control group at postoperative weeks 2 and 4.

Aqueous flare elevation after cataract surgery is likely caused by physical stress due to surgical invasion or intraocular lens implantation. This occurs when prostaglandin E2 and cytokines, including IL-6, IL-8, and IL-4, produced by macrophages and lens epithelial cells, break down the blood–aqueous barrier [6]. Nonsteroidal eye drops, which prevent prostaglandin E2 synthesis, are often used for post-cataract surgery management. The fact that HOT inhibits IL-6, IL-8, and IL-4 production suggests that it decreases aqueous flare elevation after cataract surgery by suppressing these cytokines [9-11]. Thus, HOT appears to exert its effects through mechanisms that differ from those of nonsteroidal eye drops.

Eye drops are generally used for post-cataract surgery management, but HOT could be less of a burden on patients because it is administered orally. Therefore, HOT might be a useful management option for patients post-cataract surgery. Although HOT is rarely used for ophthalmologic disease, the present results suggest a new clinical application for HOT.

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